

TRANSMITTAL LETTER			Case No. 10709/63
Serial No. 10/743,281	Filing Date December 22, 2003	Examiner N/A	Group Art Unit 1616
Inventor(s): Melikian A., et al.			
Title of Invention INHIBITORS OF HUMAN TUMOR-EXPRESSED CCXCKR2			

TO THE COMMISSIONER FOR PATENTS

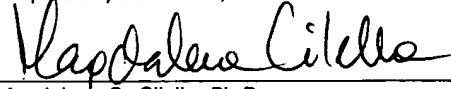
Transmitted herewith is Information Disclosure Statement (in dupl.); Form PTO-1449; Copies of the cited references A1-A57; Limited Recognition Certificate; and return postcard.

- ☐ Small entity status of this application under 37 CFR § 1.27 has been established by verified statement previously submitted.
- ☒ Applicant claims small entity status. See 37 CFR 1.27.
- ☐ Petition for a _____ month extension of time.
- ☒ No additional fee is required.
- ☐ The fee has been calculated as shown below:

				Small Entity		Other Than Small Entity		
	Claims Remaining After Amendment		Highest No. Previously Paid For	Present Extra	Rate	Add'l Fee	Rate	Add'l Fee
Total		Minus			x \$9 =		x \$18 =	
Indep.		Minus			x 43 =		x \$86 =	
First Presentation of Multiple Dep. Claim					+ \$145 =		+ \$290 =	
					Total add'l fee	\$	Total add'l fee	\$

- ☐ Please charge Deposit Account No. 23-1925 (BRINKS HOFER GILSON & LIONE) in the amount of \$_____. A duplicate copy of this sheet is enclosed.
- ☐ A check in the amount of \$_____ to cover the filing fee is enclosed.
- ☒ The Commissioner is hereby authorized to charge payment of any additional filing fees required under 37 CFR § 1.16 and any patent application processing fees under 37 CFR § 1.17 associated with this communication or credit any overpayment to Deposit Account No. 23-1925. A duplicate copy of this sheet is enclosed.
- ☒ I hereby petition under 37 CFR § 1.136(a) for any extension of time required to ensure that this paper is timely filed. Please charge any associated fees which have not otherwise been paid to Deposit Account No. 23-1925. A duplicate copy of this sheet is enclosed.

Respectfully submitted,

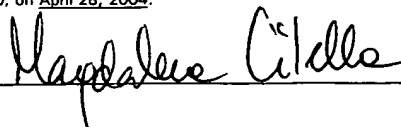

Magdalena O. Cilella, Ph.D.
Limited Recognition Certificate Enclosed
Agent of Attorney for Applicant
Customer No. 00757 - Brinks Hofer Gilson Lione

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Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on April 28, 2004.

Date: April 28, 2004

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Magdalena O. Cilella is hereby given limited recognition under 37 CFR § 10.9(b) as an employee of Brinks, Hofer, Gilson & Lione PC to prepare and prosecute patent applications wherein the patent applicant is the client of Brinks, Hofer, Gilson & Lione PC, and the attorney or agent of record in the applications is a registered practitioner who is a member of Brinks, Hofer, Gilson & Lione PC. This limited recognition shall expire on the date appearing below, or when whichever of the following events first occurs prior to the date appearing below: (i) Magdalena O. Cilella ceases to lawfully reside in the United States, (ii) Magdalena O. Cilella's employment with Brinks, Hofer, Gilson & Lione PC ceases or is terminated, or (iii) Magdalena O. Cilella ceases to remain or reside in the United States, authorized to be employed by an Employment Authorization Card issued pursuant to 8 CFR § 274a.12(c)(9).

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Group Art Unit No.: 1616

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The references now cited are the following:

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US 2002/0076710 A1	06/20/2002	Papsidero et al.

Foreign Patents

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EP 0 897 980 A2	02/24/1999	EPO
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WO 98/14480	04/09/1998	WIPO
WO 99/50461	10/07/1999	WIPO

Other Art

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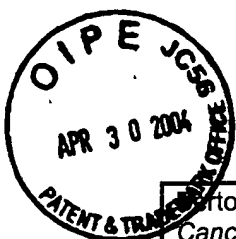
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<p>Fortolini et al., "CXCR4 Neutralization, a Novel Therapeutic Approach for Non-Hodgkin's Lymphoma¹," <i>Cancer Research</i>, 62:3106-3112 (2002).</p> <p>Dairaghi et al., "HHV8-encoded vMIP-I Selectively Engages Chemokine Receptor CCR8," <i>J. Biol. Chem.</i>, 274(31):21569-21574 (1999).</p> <p>Tatjana Dragic, "An overview of the determinants of CCR5 and CXCR4 co-receptor function," <i>J. Gen. Virol.</i>, 82:1807-1814 (2001).</p> <p>Förster et al., "Intracellular and Surface Expression of the HIV-1 Coreceptor CXCR4/Fusin on Various Leukocyte Subsets: Rapid Internalization and Recycling Upon Activation," <i>J. Immunol.</i>, 160:1522-1531 (1998).</p> <p>Gerlach et al., "Molecular Interactions of Cyclam and Bicyclam Non-peptide Antagonists with the CXCR4 Chemokine Receptor," <i>J. Biol. Chem.</i>, 276(17):14153-14160 (2001).</p> <p>Gosling et al., "Cutting Edge: Identification of a Novel Chemokine Receptor That Binds Dendritic Cell- and T Cell-Active Chemokines Including ELC, SLC, and TECK," <i>J. Immunol.</i>, 164(6):2851-2856 (2000).</p> <p>Gribble GW and Nutaitis CF, "Reactions of Sodium Borohydride in Acidic Media; XVI. N-Methylation of Amines with Paraformaldehyde/Trifluoroacetic Acid," <i>Synthesis</i>, 709 (1987).</p> <p>Kevill DN and Rissmann TJ, "Correlation of the Rates of Solvolysis of Allyl and Benzyl Arenesulphonates," <i>J. Chem. Soc. Perkin Trans. 2</i>:717-720 (1984).</p> <p>Kledal et al., "A Broad-Spectrum Chemokine Antagonist Encoded by Kaposi's Sarcoma-Associated Herpesvirus," <i>Science</i>, 277:1656-1659 (1997).</p> <p>Lee et al., "Epitope Mapping of CCR5 Reveals Multiple Conformational States and Distinct but Overlapping Structures Involved in Chemokine and Coreceptor Function," <i>J. Biol. Chem.</i>, 274(14):9617-9626 (1999).</p> <p>Lin et al., "Antiangiogenic gene therapy targeting the endothelium-specific receptor tyrosine kinase Tie2," <i>Proc. Natl. Acad. Sci. USA</i>, 95:8829-8834 (1998).</p> <p>Lance A. Liotta, "An attractive force in metastasis," <i>Nature</i>, 410:24-25 (2001).</p> <p>Mattson et al., "An Improved Method for Reductive Alkylation of Amines Using Titanium (IV) Isopropoxide and Sodium Cyanoborohydride¹," <i>J. Org. Chem.</i>, 55:2552-2554 (1990).</p> <p>Moepps et al., "Two murine homologues of the human chemokine receptor CXCR4 mediating stromal cell-derived factor 1α activation of G₁₂ are differently expressed <i>in vivo</i>," <i>Eur. J. Immunol.</i>, 27:2102-2112 (1997).</p> <p>Muller et al., "Involvement of chemokine receptors in breast cancer metastasis," <i>Nature</i>, 410:50-56 (2001).</p> <p>Bernhard Neises & Wolfgang Steglich, "Simple Method for the Esterification of Carboxylic Acids¹¹," <i>Angew. Chem. Int. Ed. Engl.</i>, 17(7):522-524 (1978).</p> <p>Neote et al., "Molecular Cloning, Functional Expression, and Signaling Characteristics of a C-C Chemokine Receptor," <i>Cell</i>, 72:415-425 (1993).</p> <p>Oppenheim et al., "Properties of the Novel Proinflammatory Supergene "Interkrine" Cytokine Family¹," <i>Annu. Rev. Immunol.</i>, 9:617-648 (1991).</p> <p>Parolin et al., "Use of Murine CXCR-4 as a Second Receptor by Some T-Cell-Tropic Human Immunodeficiency Viruses," <i>J. Virol.</i>, 72(2):1652-1656 (1998).</p> <p>Ponath et al., "Molecular Cloning and Characterization of a Human Eotaxin Receptor Expressed Selectively on Eosinophils," <i>J. Exp. Med.</i>, 183:2437-2448 (1996).</p> <p>Power et al., "Molecular Cloning and Functional Expression of a Novel CC Chemokine Receptor cDNA from a Human Basophilic Cell Line," <i>J. Biol. Chem.</i>, 270(33):19495-19500 (1995).</p> <p>Pulaski et al., "Cooperativity of <i>Staphylococcal aureus</i> Enterotoxin B Superantigen, Major Histocompatibility Complex Class II, and CD80 for Immunotherapy of Advanced Spontaneous Metastases in a Clinically Relevant Postoperative Mouse Breast Cancer Model¹," <i>Cancer Research</i>, 60:2710-2715 (2000).</p> <p>Thomas J. Schall, "Biology of the Rantes/sis Cytokine Family," <i>Cytokine</i>, 3(3):165-183 (1996).</p> <p>Watanabe et al., "The Selective Amination of Carbonyl Compounds Using Iron Pentacarbonyl," <i>Tetrahedron Lett.</i>, No. 22:1879-1880 (1974).</p> <p>Wegner et al., "Genomic Organization and Functional Characterization of the Chemokine Receptor CXCR4, a Major Entry Co-receptor for Human Immunodeficiency Virus Type 1," <i>J. Biol. Chem.</i>, 273(8):4754-4760 (1998).</p>
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FORM PT-1449	SERIAL NO. 10/743,281	CASE NO. 10709/63
LIST OF PATENTS AND PUBLICATIONS FOR APPLICANT'S INFORMATION DISCLOSURE STATEMENT	FILING DATE December 22, 2003	GROUP ART UNIT 1616
(use several sheets if necessary)		APPLICANT(S): Melikian A., et al.

REFERENCE DESIGNATION

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	A19	US 2002/0061599 A1	05/23/2002	Elling et al.		
	A20	US 2002/0061834 A1	05/23/2002	Rosen et al.		
	A21	US 2002/0064770 A1	05/30/2002	Nestor, Jr. et al.		
	A22	US 2002/0076710 A1	06/20/2002	Papsidero et al.		

FOREIGN PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER <small>Number-Kind Code (if known)</small>	DATE	COUNTRY	CLASS/ SUBCLASS	TRANSLATION YES OR NO
	A23	EP 0 897 980 A2	02/24/1999	EPO		Yes
	A24	WO 98/11218	03/19/1998	WIPO		Yes
	A25	WO 98/14480	04/09/1998	WIPO		Yes
	A26	WO 99/50461	10/07/1999	WIPO		Yes

EXAMINER INITIAL	OTHER ART – NON PATENT LITERATURE DOCUMENTS <small>(Include name of author, title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date page(s), volume-issue number(s), publisher, city and/or country where published.</small>	
	A27	Abdel-Magid et al., "Reductive Amination of Aldehydes and Ketones by Using Sodium Triacetoxyborohydride ¹ ," <i>Tetrahedron Lett.</i> , 31:5595-5598 (1990).
EXAMINER		DATE CONSIDERED

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FORM PTO-1449	SERIAL NO. 10/743,281	CASE NO. 10709/63
LIST OF PATENTS AND PUBLICATIONS FOR APPLICANT'S INFORMATION DISCLOSURE STATEMENT	FILING DATE December 22, 2003	GROUP ART UNIT 1616
(use several sheets if necessary)		APPLICANT(S): Melikian A., et al.

EXAMINER INITIAL	OTHER ART – NON PATENT LITERATURE DOCUMENTS (Include name of author, title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date page(s), volume-issue number(s), publisher, city and/or country where published.	
	A28	Babcock et al., "Ligand Binding Characteristics of CXCR4 Incorporated into Paramagnetic Proteoliposomes," <i>J. Biol. Chem.</i> , 276(42):38433-38440 (2001).
	A29	Baribaud et al., "Antigenically Distinct Conformations of CXCR4," <i>J. Virol.</i> , 75(19):8957-8967 (2001).
	A30	Barney et al., "A Convenient Synthesis of Hindered Amines and α -Trifluoromethylamines from Keytones," <i>Tetrahedron Lett.</i> , 31:5547 (1990).
	A31	Bertolini et al., "Endostatin, an antiangiogenic drug, induces tumor stabilization after chemotherapy or anti-CD20 therapy in a NOD/SCID mouse model of human high-grade non-Hodgkin lymphoma," <i>Blood</i> , 1(96):282-287 (2000).
	A32	Bertolini et al., "CXCR4 Neutralization, a Novel Therapeutic Approach for Non-Hodgkin's Lymphoma ¹ ," <i>Cancer Research</i> , 62:3106-3112 (2002).
	A33	Dairaghi et al., "HHV8-encoded vMIP-I Selectively Engages Chemokine Receptor CCR8," <i>J. Biol. Chem.</i> , 274(31):21569-21574 (1999).
	A34	Tatjana Dragic, "An overview of the determinants of CCR5 and CXCR4 co-receptor function," <i>J. Gen. Virol.</i> , 82:1807-1814 (2001).
	A35	Förster et al., "Intracellular and Surface Expression of the HIV-1 Coreceptor CXCR4/Fusin on Various Leukocyte Subsets: Rapid Internalization and Recycling Upon Activation," <i>J. Immunol.</i> , 160:1522-1531 (1998).
	A36	Gerlach et al., "Molecular Interactions of Cyclam and Bicyclam Non-peptide Antagonists with the CXCR4 Chemokine Receptor," <i>J. Biol. Chem.</i> , 276(17):14153-14160 (2001).
	A37	Gosling et al., "Cutting Edge: Identification of a Novel Chemokine Receptor That Binds Dendritic Cell- and T Cell-Active Chemokines Including ELC, SLC, and TECK," <i>J. Immunol.</i> , 164(6):2851-2856 (2000).
	A38	Gribble GW and Nutaitis CF, "Reactions of Sodium Borohydride in Acidic Media; XVI. N-Methylation of Amines with Paraformaldehyde/Trifluoroacetic Acid," <i>Synthesis</i> , 709 (1987).
	A39	Kevill DN and Rissmann TJ, "Correlation of the Rates of Solvolysis of Allyl and Benzyl Arenesulphonates," <i>J. Chem. Soc. Perkin Trans. 2</i> :717-720 (1984).
	A40	Kledal et al., "A Broad-Spectrum Chemokine Antagonist Encoded by Kaposi's Sarcoma-Associated Herpesvirus," <i>Science</i> , 277:1656-1659 (1997).
	A41	Lee et al., "Epitope Mapping of CCR5 Reveals Multiple Conformational States and Distinct but Overlapping Structures Involved in Chemokine and Coreceptor Function," <i>J. Biol. Chem.</i> , 274(14):9617-9626 (1999).
	A42	Lin et al., "Antiangiogenic gene therapy targeting the endothelium-specific receptor tyrosine kinase Tie2," <i>Proc. Natl. Acad. Sci. USA</i> , 95:8829-8834 (1998).
	A43	Lance A. Liotta, "An attractive force in metastasis," <i>Nature</i> , 410:24-25 (2001).
	A44	Mattson et al., "An Improved Method for Reductive Alkylation of Amines Using Titanium (IV) Isopropoxide and Sodium Cyanoborohydride ¹ ," <i>J. Org. Chem.</i> , 55:2552-2554 (1990).
	A45	Moepps et al., "Two murine homologues of the human chemokine receptor CXCR4 mediating stromal cell-derived factor 1 α activation of G ₁₂ are differently expressed <i>in vivo</i> ," <i>Eur. J. Immunol.</i> , 27:2102-2112 (1997).

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FORM PTO-1449	SERIAL NO. 10/743,281	CASE NO. 10709/63
LIST OF PATENTS AND PUBLICATIONS FOR APPLICANT'S INFORMATION DISCLOSURE STATEMENT	FILING DATE December 22, 2003	GROUP ART UNIT 1616
(use several sheets if necessary)	APPLICANT(S): Melikian A., et al.	

EXAMINER INITIAL	OTHER ART – NON PATENT LITERATURE DOCUMENTS (Include name of author, title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date page(s), volume-issue number(s), publisher, city and/or country where published.	
	A46	Muller et al., "Involvement of chemokine receptors in breast cancer metastasis," <i>Nature</i> , 410:50-56 (2001).
	A47	Bernhard Neises & Wolfgang Steglich, "Simple Method for the Esterification of Carboxylic Acids ^[1] ," <i>Angew. Chem. Int. Ed. Engl.</i> , 17(7):522-524 (1978).
	A48	Neote et al., "Molecular Cloning, Functional Expression, and Signaling Characteristics of a C-C Chemokine Receptor," <i>Cell</i> , 72:415-425 (1993).
	A49	Oppenheim et al., "Properties of the Novel Proinflammatory Supergene "Interkrine" Cytokine Family ¹ ," <i>Annu. Rev. Immunol.</i> , 9:617-648 (1991).
	A50	Parolin et al., "Use of Murine CXCR-4 as a Second Receptor by Some T-Cell-Tropic Human Immunodeficiency Viruses," <i>J. Virol.</i> , 72(2):1652-1656 (1998).
	A51	Ponath et al., "Molecular Cloning and Characterization of a Human Eotaxin Receptor Expressed Selectively on Eosinophils," <i>J. Exp. Med.</i> , 183:2437-2448 (1996).
	A52	Power et al., "Molecular Cloning and Functional Expression of a Novel CC Chemokine Receptor cDNA from a Human Basophilic Cell Line," <i>J. Biol. Chem.</i> , 270(33):19495-19500 (1995).
	A53	Pulaski et al., "Cooperativity of <i>Staphylococcal aureus</i> Enterotoxin B Superantigen, Major Histocompatibility Complex Class II, and CD80 for Immunotherapy of Advanced Spontaneous Metastases in a Clinically Relevant Postoperative Mouse Breast Cancer Model ¹ ," <i>Cancer Research</i> , 60:2710-2715 (2000).
	A54	Thomas J. Schall, "Biology of the Rantes/sis Cytokine Family," <i>Cytokine</i> , 3(3):165-183 (1996).
	A55	Watanabe et al., "The Selective Amination of Carbonyl Compounds Using Iron Pentacarbonyl," <i>Tetrahedron Lett.</i> , No. 22:1879-1880 (1974).
	A56	Wegner et al., "Genomic Organization and Functional Characterization of the Chemokine Receptor CXCR4, a Major Entry Co-receptor for Human Immunodeficiency Virus Type 1," <i>J. Biol. Chem.</i> , 273(8):4754-4760 (1998).
	A57	Yoshida et al., "Identification of Single C Motif-1/Lymphotactin Receptor XCR1," <i>J. Biol. Chem.</i> , 273(26):16551-16554 (1998).

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